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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/514,113 02/28/00 DEAN

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EXAMINER

HM22/0302

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ART UNIT

PAPER NUMBER

1655

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03/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/514,113

Applicant(s)

DEAN ET AL.

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-76 is/are pending in the application.
- 4a) Of the above claim(s) 50-76 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

Drawings

1. The drawings remain objected to for reasons of record; see the PTO-948 that was attached to Paper No. 6. Acknowledgement is made of applicant's willingness to file corrected drawings upon notification of allowable subject matter.

Specification

2. The use of the trademark TRITON has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing rolling circle amplification with the use of a primer that comprises abasic nucleotides, does not reasonably provide enablement for the use of other forms of amplification (e.g., claims 19 and 31) nor for the use of other modified nucleotides, e.g., those

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identified in claims 10 and 41. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided

The amount of guidance provided is limited to the use of abasic nucleotides in a primer sequence that is in turn used in rolling circle amplification. While other forms of amplification are identified explicitly, as well as other modified or derivatized nucleotides are identified, the specification does not provide the reaction conditions under which they would be appropriately incorporated into the primer sequence. Assuming *arguendo*, that one of skill in the art would have been able to incorporate these nucleotides into a primer sequence, a point that the Office does not concede, the specification does not provide sufficient guidance as to how they are to be used.

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The Presence or Absence of Working Examples

The specification provides but two examples, pages 20-24, and they are both limited to the use of abasic nucleotides in a primer sequences subsequently used in rolling circle amplification. The reaction conditions set forth in the specification are specific to rolling circle amplification and have also been found to be specific to the use of abasic nucleotides. Accordingly, the specific disclosures do not enable a generic method of using any type of template-deficient oligonucleotide in any form of amplification, regardless of the heterogeneity of the reaction. Further, the specification has not been found to provide sufficient guidance as to how prior art methods of amplification are to be adapted or modified so to enable the use of any template-deficient oligonucleotide. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

“ ‘[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.’ *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) (‘[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.’).

“Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that ‘a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.’) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. “It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385,

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231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

For the above reasons, and in the absence of convincing evidence to the contrary, applicant is urged to consider narrowing the scope of the claims to those embodiments adequately supported by the disclosure.

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the prior art is severely limited to the use of template-deficient oligonucleotide. As shown below, the use of abasic nucleotides was known.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have sufficient breadth of scope so to encompass the use of virtually any modified nucleotide, e.g., claims 10 and 41, in a template-deficient oligonucleotide in virtually any form of amplification, including, but necessarily limited to those set forth in claims 19 and 31, be it for a single target sequence or multiplex, *in situ* or *in vitro*.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1, 2, 5, 11, 20, 21, 23, 28, 32, 36, 39, 41, 42, 43, 44, 46, and 49 rejected under 35 U.S.C. 102(a, e) as being anticipated by Wallace.

7. Wallace, column 9, third and fourth paragraphs, disclose the use of abasic nucleotides in primer used in an amplification reaction. The teaching of "primers that contain non-replicable

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and/or cleavable elements" (column 9, lines 18-19) has been interpreted as there being a plurality of such nucleotides in a primer. Also, column 9, lines 32-33, teaches the presence of "a residue" in a primer. Accordingly, Wallace is considered to teach the use of one or more such abasic nucleotides.

8. While Wallace teaches that the preferred embodiment does not have the modified nucleotide "at the terminal residue of any of the primers" such a teaching does point to having the modified nucleotide close to the 5' terminus.

9. Claims 1, 3, 5, 11, 13, 14, 15, 16, 19, 20, 23-25, 28-32, 34, 36, 37, 41-43, and 46-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Todd et al.

Todd et al., column 11, Example 3, discloses the use of chimeric primers (contain both DNA and RNA, applicant's ribonucleotides) in a PCR reaction. Todd et al., teaches explicitly of there being "one or two" of these residues present in the chimera. This meets a limitation of claims 1, 3, 5, 11, 13, 14, 15, 16, 19, 20, 23-25, 28-32, 34, 36, 37, 41-43, and 46-49.

Conclusion

10. Rejections which appeared in the prior Office action and which have not been repeated hereinabove, have been withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
February 28, 2001